EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Richard Barth on August 25, 2008.

The Election/Restriction requirement is withdrawn. The claims are directed to an allowable product. Therefore, **the restriction requirement as set forth in the Office action mailed on November 28, 2007 is hereby withdrawn**. In view of the withdrawal of the restriction requirement as to the rejoined inventions, applicant(s) are advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, a claim that is allowable in the present application, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Once the restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. See *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Any objection or rejection of record not specifically addressed herein is withdrawn.

The application has been amended as follows:

The specification has been amended as follows:

Page 13, ¶1, lines 4-10 has been amended by replacing the paragraph. The paragraph now reads:

--- Bacillolysin MA was isolated and purified from *Bacillus megaterium* A9542 strain according to the following method. *Bacillus megaterium* A9542 was deposited on March 21, 2001 in the Ministry of Economic Trade and Industry Agency of Industrial Science and Technology, National Institute of Bioscience and Human Technology (presently the International Patent Organism Depository (IPOD), National Institute of Advanced Industrial Science and Technology (AIST), Tsukuba Central 6,1-1-1 Higashi, Tsukuba, Ibaraki, 305-8566, Japan) and was assigned the deposit No. FERM P-18268. ---

The claims have been amended as follows:

Claims 1-14. (canceled)

Claim 15. An affinity trap reactor comprising:

(a) an enzyme, wherein said enzyme is the protease bacillolysin MA obtained from *Bacillus megaterium*;

(b) a molecule that specifically binds with a substrate of said enzyme, said molecule selected from the group consisting of lysine and hirudine; and

(c) a support,

wherein each of said enzyme (a) and said molecule (b) are immobilized to said support (c).

Claim 16. The affinity trap reactor of claim 15, wherein the substrate is plasminogen and the molecule that specifically binds with said substrate is lysine.

Claim 17. The affinity trap reactor of claim 15, wherein the substrate is prothrombin and the molecule that specifically binds with said substrate is hirudine.

Claim 18. The affinity trap reactor of claim 15, wherein the support (c) is selected from the group consisting of a porous silica bead, cellulose, agarose, cross-linked dextran, and cross-linked polyacrylamide.

Claim 19. The affinity trap reactor of claim 18, wherein the support (c) is agarose and wherein said agarose is an agarose gel.

Claim 20. The affinity trap reactor of claim 19, wherein the molecule (b) is lysine.

Claim 21. The affinity trap reactor of any one of claims 15-20, wherein the *Bacillus megaterium* is *Bacillus megaterium* strain A9542.

Claim 22. The affinity trap reactor of claim 20, wherein the affinity trap reactor is produced by the method comprising:

(i) contacting an agarose gel with an HCl solution, wherein said gel is an activated agarose gel activated by contacting with a cyanogen halide;

(ii) providing a bicarbonate buffer containing isopropyl alcohol;

(iii) washing said agarose gel of step (i) with said bicarbonate buffer of step (ii) thereby providing a washed gel; and,

(iv) contacting said washed gel with a solution comprising bacillolysin MA enzyme and with a solution comprising L-lysine hydrochloride, wherein contacting said washed gel with said enzyme and with said lysine provides an affinity trap reactor, said reactor comprising each of said enzyme and said lysine immobilized to said washed gel.

Claim 23. A single-stage process of obtaining BL-angiostatin from a plasminogen-containing biological sample, the method comprising:

(i) providing the affinity trap reactor of claim 16;

(ii) applying a biological sample containing plasminogen to said trap reactor;

(iii) contacting the bacillolysin MA enzyme of said trap reactor with said plasminogen at a temperature of 0 to 50°C, in the presence of isopropyl alcohol, and in the absence of calcium ions, thereby providing BL-angiostatin; and

(iv) eluting said BL-angiostatin formed by the reaction of the bacillolysin MA and the plasminogen of step (iii) thereby obtaining BL-angiostatin.

Claim 24. A single-stage process of obtaining BL-angiostatin from a plasminogen-containing biological sample, the method comprising:

(i) providing the affinity trap reactor of claim 19;

(ii) applying a biological sample containing plasminogen to said trap reactor;

(iii) contacting the bacillolysin MA enzyme of said trap reactor with said plasminogen at a temperature of 0 to 50°C, in the presence of isopropyl alcohol, and in the absence of calcium ions, thereby providing BL-angiostatin; and

(iv) eluting said BL-angiostatin formed by the reaction of the bacillolysin MA and the plasminogen of step (iii), thereby obtaining BL-angiostatin.

Claim 25. The process according to any one of claims 23 or 24, wherein in step (iii) the temperature is 4 to 25°C.

Remarks (Deposit of Microorganism)

The invention appears to employ a specific strain of *B.megaterium* (FERM P-18268). The specification has been amended to clarify the deposit of the organism; however, it remains unclear from the record if the starting materials were readily available to the public at the time of invention. Thus, it is not clear if the deposit meets all

of the criteria set forth in the deposit of biological material under 37 CFR 1.801-1.809. Applicant is herein notified that the above claims have been found to be otherwise in condition for allowance, thus Applicant is required to provide appropriate assurance of compliance with the requirements so as to comply with 35 USC 112, 1st ¶ and 37 CFR 1.801-1.809.

For compliance with the rule, it must be averred that deposited material has been accepted for deposit under the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the purpose of Patent Procedure (e.g. see 961 OG 21, 1977) and that all restrictions on the availability to the public of the material so deposited will be irrevocably removed upon the granting of a patent (MPEP 2403).

Any information which comes to an applicant's attention *during the prosecution of this application*, must be entered in the record or otherwise be brought to the attention of the Office by the Applicant as defects in the deposit of biological material cannot be cured by reissue after the grant of a patent.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to AARON J. KOSAR whose telephone number is (571)270-3054. The examiner can normally be reached on Monday-Thursday, 7:30AM-5:00PM, ALT. Friday,EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Aaron J Kosar/
Examiner, Art Unit 1651

/Sandra Saucier/
Primary Examiner, Art Unit 1651